UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,695	11/21/2006	Toshihiro Tanaka	P29373	4545

7055 7590 04/26/2011

GREENBLUM & BERNSTEIN, P.L.C.
1950 ROLAND CLARKE PLACE
RESTON, VA 20191

EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
04/26/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,695	TANAKA ET AL.	
	Examiner	Art Unit	
	STEPHEN KAPUSHOC	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-13* is/are pending in the application.

4a) Of the above claim(s) *5-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 5-13 are pending.
Claims 5-13 remain withdrawn from examination as detailed in the Office Action of 01/26/2009.
Claim 1 is examined on the merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/25/2010 has been entered.

This Office Action is in reply to Applicants' correspondence of 05/25/2010.
Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put this application in condition for allowance. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.
This Action is **NON-FINAL**.

Please note: The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

1. The Declaration of Kouichi Ozaki under 37 CFR 1.132 filed 05/25/2010 is insufficient to overcome the rejection of claim 1 for lack of enablement based upon 35 USC 112 1st paragraph as set forth in the last Office action because: The declaration

asserts that the cited art of Asselbergs et al (2007) supports the correlation between the 3279 SNP in galectin-2 with myocardial infarction risk in a population separate from the population studied in the specification as originally filed. However, in analyzing the data presented in Asselbergs et al, the data is not convincing to support the enablement of the instantly claimed methods, where the data of Asselbergs et al does not support the required association in any of the male populations examined in that publication (i.e.: Table 2 on page 294), and the reference indicates 'a significant gender interaction' (p.294, bottom of right col.). Additionally, the newly cited reference of Li et al (2010) (as cited in the rejection below) provides a meta analysis of all available data regarding the 3279 SNP and heart disease; and taking into account all the available data Li et al reaches the conclusion that there is not in fact a significant association between the 3279 SNP and heart disease. For these reasons, the Declaration is not sufficient to overcome the rejection, and the rejection is maintained in this Office Action.

Claim Rejections - 35 USC § 112 1st ¶ - Enablement

2. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature of the invention and breadth of the claims

The instant claims are drawn to methods for determining an increased risk of myocardial infarction in humans.

The claims require knowledge of a correlative association between a C at position 3279 of SEQ ID NO: 1 and an increased risk of myocardial infarction.

Direction provided by the specification and working example

The specification provides an example of the identification of a polymorphism in the human galectin-2 gene, where the polymorphic content is either a C or a T at position 3279 of SEQ ID NO: 1 (p.6-7).

The specification teaches (p.16; p.20-21), the analysis of the polymorphisms in case and control populations to study the association of the SNP content with the presence of myocardial infarction (MI). The specification asserts that the presence of the TT genotype at the position in both alleles of the galectin-2 gene is indicative of a decreased risk of MI (p.20).

The specification does not provide any examples of the analysis of any other arteriosclerotic diseases other than MI. There is no validation analysis of any additional population other than the subjects as presented in Table 1 on page 21 of the specification.

State of the art, level of skill in the art, and level of unpredictability

While the state of the art with regard to the detection of any particular nucleotide sequence is high, the unpredictability with regard to the association of any particular sequence with a particular phenotype, or the identification of any nucleotide sequence has having a particular functionality, is even higher. The unpredictability is demonstrated by the prior art and the post-filing art.

Because the nature of the claimed methods requires knowledge of a robust and reliable association between nucleotide content and disease risk, it is relevant to point out the unpredictable nature of any mutation association study. As evidence of the unpredictability of gene association studies, Lucentini (2004) teaches that it is strikingly common for follow-up studies to find gene-disease associations wrong (left column, 3rd paragraph). Lucentini teaches that two recent studies found that typically when a finding is first published linking a given gene to a disease there is only roughly a one-third chance that the study will reliably confirm the finding (left column, 3rd paragraph). Lucentini teaches that bigger sample sizes and more family-based studies, along with revising statistical methods, should be included in the gene association studies (middle column, 1st complete paragraph). Additionally, Hegele (2002) teaches the general unpredictability in associating any genotype with a phenotype. Hegele teaches that often initial reports of an association are followed by reports of non-replication and refutation (p.1058, right col., lns.24-30). Hegele provides a table indicating some desirable attributes for genetic association studies (p.1060), and includes choosing an appropriate significance threshold (see 'Minimized type 1 error (FP)') and replication of results in independent samples (see 'Replication'). Additionally, Hegele teaches the desirability of a likely functional consequence predicted by a known or putative functional domain.

The unpredictability as generally described by Lucentini and by Hegele, as cited above, is particularly relevant considering the teachings of the post-filing art. For example, the post filing-art teaches the analysis of the same SNP in the galectin-2 gene

and a lack of association with MI. Mangino et al (2007) teach that the SNP rs7291467 (the same SNP of the instant application) is not associated with MI in a Caucasian population (p.114 left col.). Similarly, Sedlacek et al (2007) teaches (p.1000, Table 3) that there is no significant association between the same SNP and MI in two German populations. Finally, Kimura et al teaches that there was no association of the SNP with MI in a Japanese population or a Korean population (p.267, left col.; Table 3). It is thus unpredictable as to weather or not the asserted association of the instant specification would in fact reliably or robustly be reproduced in any other different population.

Additionally, Li et al (2010) provides a meta analysis of all available data, in numerous diverse study population, related to the galectin-2 3279 SNP and heart disease. The reference concludes (e.g.: Figures 4 and 5) that there is no statistically significant, reliable association between the 3279 SNP content and heart disease risk (e.g.: p.434 - Results).

Quantity of experimentation required

A large and prohibitive amount of experimentation would have to be performed in order to make and use the claimed invention. Such experimentation would include large case:control studies to establish whether or not the asserted associations are reliable and robust in any subject population of interest. Such experimentation would be extensive. Even if one were to carry out such experimentation, there is no assurance that a reliable and consistent association of genetic content with MI would be identified.

Conclusion

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the guidance provided by the applicant and the specific examples, it is the conclusion that an undue amount of experimentation would be required to make and use the invention.

Response to Remarks

Applicants have traversed the rejection of claims under 35 USC 112 1st ¶ for lack of enablement. Applicants' arguments (p.2-3 of the Remarks of 05/25/2010) have been fully and carefully considered but are not found to be persuasive to withdraw the rejection. Applicants remarks depend on the evidence presented in the Declaration which asserts that the Asselbergs reference supports the required genotype:phenotype association. As addressed earlier in this Office Action, the Declaration is not sufficient to overcome the rejection; additionally it is noted that the newly cited Li et al reference supports the Examiner's position that when the available evidence is taken together, the evidence does not support the required association.

The rejection as set forth is **MAINTAINED.**

Conclusion

3. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Stephen Kapushoc/
Primary Examiner, Art Unit 1634